Clinical Pharmacology & Toxicology Pearl of the Week

~ Acute Iron Poisoning ~

Iron Pharmacology

- ✓ Iron is absorbed in its ferrous state (Fe^{2+}) within the proximal small bowel primarily via DMT-1 along the apical surface and via Ferroportin along the basolateral surface.
- ✓ The protein Hepcidin regulates transport protein expression and prevents excessive absorption of iron.
- ✓ Physiologic regulation of iron absorption becomes dysfunctional in massive ingestion
- ✓ There exist no physiologic mechanisms for iron excretion

Iron Toxicity

- ✓ Iron exerts toxic effect through lipid peroxidation and free radical production culminating in caustic mucosal injury and decoupling of oxidative phosphorylation
- ✓ Life threatening toxicity may develop with doses greater than 60mg/kg of elemental iron
- ✓ A **Serum Iron Concentration (SIC)** at 4-6 hours post ingestion is prognostically relevant **(See Figure 2)**
- ✓ There are five classically described phases of toxicity:

Common sources of Iron (Figure 1)

- Ferrous Gluconate – 12% elemental iron
- Ferrous Sulfate – 20% elemental iron
- Ferrous Fumarate – 33% elemental iron

SIC Levels and associated morbidity (Figure 2)

- SIC < 63 umol/L – Minimal symptoms
- SIC 63 – 90 umol/L – Moderate toxicity
- SIC 90 – 180 umol/L – Serious toxicity
- SIC > 180 umol/L – Life-threatening toxicity

Gastrointestinal phase (~6 hours post-ingestion)
- Secondary to caustic mucosal injury
- Abdominal pain, nausea, vomiting

Latent phase (6-24 hours post-ingestion)
- Symptom resolution due to iron redistribution
- Often absent in severe toxicity however presence does not preclude deterioration

Shock and metabolic acidosis (12-48 hours post-ingestion)
- Anion gap metabolic acidosis with both distributive and cardiogenic shock
- Progressive multi-organ failure (ARDS, coagulopathy, renal failure)

Hepatotoxicity (24-96 hours post-ingestion)
- Massive hepatic iron deposition leads to acute hepatic necrosis

Bowel Obstruction (2-8 weeks post-ingestion)
- Secondary to caustic bowel injury and subsequent luminal scarring and stenosis

Management

- ✓ Obtain SIC 4-6 hours post ingestion and calculate the per-kilogram ingestion of elemental iron. Asymptomatic patients with a SIC < 90 umol/L and a normal abdominal x-ray may be discharged
- ✓ **Decontamination:** Whole bowel irrigation may play a role in large volume ingestion. Activated charcoal is **not** effective at binding iron.
- ✓ **Antidote:** Deferoxamine is a chelating agent that binds ferric iron in the blood to form the water soluble compound ferrioxamine which can be renally excreted. Conventional dosing starts at 15mg/kg/hr.
- ✓ **Indications for deferoxamine include:**
  - Severe signs and symptoms including shock, metabolic acidosis, pills on abdominal xray
  - SIC > 90 umol/L
- ✓ Hypotension and ARDS may complicate administration of deferoxamine. Consultation with a medical toxicologist is indicated prior to initiating treatment

The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Click HERE for clinical issues the CP service can assist with.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414, and select option 1